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(54) **DISPOSABLE TEST STRIPS FOR DETERMINATION OF BLOOD ANALYTES, AND METHODS FOR MAKING SAME**

WEGWERFBARE TESTSTREIFEN ZUR BESTIMMUNG VON BLUTBESTANDTEILEN UND VERFAHREN ZUR HERSTELLUNG DERSELBEN

BANDES DE TEST A JETER POUR LA MESURE DE LA CONCENTRATION D'ANALYTES SANGUINS, ET PROCEDESS DE FABRICATION

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Description

BACKGROUND OF THE INVENTION

[0001] This application relates to disposable test strips for use in electrochemical determinations of blood analyses such as glucose, and to methods for use in making such strips.

[0002] Glucose monitoring is a fact of everyday life for diabetic individuals, and the accuracy of such monitoring can literally mean the difference between life and death. To accommodate a normal life style to the need for frequent monitoring of glucose levels, a number of glucose meters are now available which permit the individual to test the glucose level in a small amount of blood.

[0003] Many of these meters detect glucose in a blood sample electrochemically, by detecting the oxidation of blood glucose using an enzyme such as glucose oxidase provided as part of a disposable, single use electrode system. Examples of devices of this type are disclosed in European Patent No. 0 127 958, and US Patents Nos. 5,141,868, 5,286,362, 5,288,636, and 5,437,999 which are incorporated herein by reference.

[0004] In general, existing glucose test strips for use in electrochemical meters comprise a substrate, working and reference electrodes formed on the surface of the substrate, and a means for making connection between the electrodes and the meter. The working electrode is coated with an enzyme capable of oxidizing glucose, and a mediator compound which transfers electrons from the enzyme to the electrode resulting in a measurable current when glucose is present. Representative mediator compounds include ferricyanide, metallocene compounds such as ferrocene, quinones, phenazinium salts, redox indicator DCPIP, and imidazole-substituted osmium compounds.

[0005] Working electrodes of this type have been formulated in a number of ways. For example, mixtures of conductive carbon, glucose oxidase and a mediator have been formulated into a paste or ink and applied to a substrate. EP 0 127 958 and US 5,286,362. In the case of disposable glucose strips, this application is done by screen printing in order to obtain the thin layers suitable for a small flat test strip. The use of screen printing, however, introduces problems to the operation of the electrode.

[0006] Unlike a thicker carbon paste electrode which remains fairly intact during the measurement, screen printed electrodes formed from carbon pastes or inks are prone to break up on contact with the sample. The consequences of this breakup are two-fold. Firstly, the components of the electrode formulation are released into solution. Once these components drift more than a diffusion length away from the underlying conductive layer, they no longer contribute toward the measurement, but in fact diminish the response by depleting inwardly-diffusing analyte. Secondly, the breakup of the screen printed electrode means that the effective electrode area is falling over time.

[0007] The combination of these two effects results in current transients which fall rapidly from an initial peak over the period of the measurement, and a high sensitivity to oxygen which quickly competes with the mediator for the enzyme. This fact is clearly demonstrated by the much lower currents measured in blood samples than in plasma samples or other aqueous media, and can result in erroneous readings. A further consequence is that the transients are often "lumpy" as the electrode breaks up in a chaotic manner. Lumpy transients either give rise to erroneous readings or rejected strips, neither of which are acceptable.

[0008] In addition to the potential for electrode breakup of screen-printed carbon-based electrodes, known electrodes used in disposable glucose test strips have been kinetically-controlled, i.e., the current depends on the rate of conversion of glucose by the enzyme. Because the response measured by the instrument represents a balance between the reactions of enzyme and mediator, enzyme and glucose and enzyme and oxygen, and because each of these reactions has its own dependence on temperature, the response of a kinetically-controlled test strip is very sensitive to the temperature of the sample. Substantial variation in the measured glucose value can therefore occur as a result of variations in sample handling.

[0009] Because of the importance of obtaining accurate glucose readings to the well-being of a patient using the meter and disposable test strips, it would be highly desirable to have a glucose test strip which did not suffer from these drawbacks, and which therefore provided a more consistent and reliable indication of actual blood glucose values, regardless of actual conditions. It is therefore an object of the present invention to provide disposable glucose test strips which are not prone to electrode breakup on contact with a sample.

[0010] It is a further object of this invention to provide glucose test strips which provide a glucose reading that is essentially independent of the hematocrit of the sample.

[0011] It is a further object of the present invention to provide glucose test strips which are substantially independent of temperature over a range between normal body temperature and room temperature.

[0012] It is a further object of the invention to provide test strips which provide a substantially flat current transient, without significant decay for periods of at least 10 seconds after the peak current level is obtained.

SUMMARY OF THE INVENTION

[0013] The present invention provides a disposable test strip having the features set out in claim 1 of the accompanying claims.

[0014] It also provides a method for making the aforesaid test strip which has the features set out in claim 19

of the accompanying claims.

[0015] In the above test, the working electrode comprises a conductive base layer disposed on the substrate and a preferably non-conductive coating disposed over the conductive base layer. In the case of a glucose test strip, the non-conductive coating comprises a filler which has both hydrophobic and hydrophilic surface regions, an enzyme effective to oxidize glucose, e.g., glucose oxidase, and a mediator effective to transfer electrons from the enzyme to the conductive base layer. The filler is preferably selected to have a balance of hydrophobicity and hydrophilicity such that on drying it forms a two-dimensional network on the surface of the conductive base layer. Preferred fillers are non-conductive silica fillers. The response of this test strip is dependent on the diffusion rate of glucose, not on the rate at which the enzyme can oxidize glucose, such that the performance of the test strip is essentially temperature independent over relevant temperature ranges. Further, the silica appears to form a two-dimensional network which excludes red blood cells, thus rendering the test strip substantially insensitive to the hematocrit of the patient.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016]

Pigs. 1A and 1B show an electrode structure useful in a disposable test strip in accordance with the invention;

Fig. 2 shows a test strip in accordance with the invention;

Figs. 3A - 3C show the current measured as a function of glucose concentration for three different hematocrit levels;

Fig. 4 shows the relationship of the glucose-concentration dependence of the measured current as a function of hematocrit;

Figs. 5A - 5C show the current measured as a function of glucose in blood and a control solution for three different conductive base layers;

Figs. 6A and 6B show the current measured as a function of glucose at two different temperatures;

Fig. 7 shows a further embodiment of a glucose test strip according to the invention; and

Figs 8A and 8B show current transients observed using a test strip according to the invention and a commercial carbon-based test strip.

DETAILED DESCRIPTION OF THE INVENTION

[0017] Figs. 1A and 1B show electrodes useful in a disposable test strip in accordance with the invention. As shown, the electrodes are formed on a substrate 10. On the substrate 10 are placed a conductive base layer 16, a working electrode track 15, a reference electrode track 14 ending in reference electrode 14', and conductive contacts 11, 12, and 13. An insulating mask 18 is then formed, leaving a portion of the conductive base layer 16, and the contacts 11, 12 and 13 exposed. A region of a working coating 17 is then applied over the insulating mask 18 to make contact with conductive base layer 16.

[0018] The assembly shown in Fig. 1 provides a fully functional assembly for the measurement of a blood analyte when connected to a meter. Advantageously, however, the electrode strips of the invention are finished by applying a polyester mesh 21 over the region of the working coating 17 of the electrode assembly 22, and then a top cover 23 to prevent splashing of the blood sample. (Fig. 2) The polyester mesh acts to guide the sample to the reference electrode 14', thereby triggering the device and initiating the test.

[0019] The substrate 10 used in making the test strips of the invention can be any non-conducting, dimensionally stable material suitable for insertion into a glucose test meter. Suitable materials include polyester films, for example a 330 micron polyester film, and other insulating substrate materials.

[0020] The working electrode track 15, the reference electrode track 14, and conductive contacts 11, and 12 can be formed from essentially any conductive material including silver, Ag/AgCl, gold, or platinum/carbon.

[0021] The conductive base layer 16 is preferably formed from conductive carbon. Preferred conductive carbon are ERCON ERC1, ERCON ERC2 and Acheson Carbon Electrodag 423. Carbon with these specifications is available from Ercon Inc. (Waltham, Massachusetts, USA), or Acheson Colloids, (Princes Rock, Plymouth, England). The conductive base layer 16 makes contact with working electrode track 15, and is close to, but not contacting the end of reference electrode track 14.

[0022] The insulating layer 18 can be formed from polyester-based printable dielectric materials such as ERCON R488-B(HV)-B2 Blue. The top cover 23 is suitably formed from a polyester strip or a "hot melt" coated plastic.

[0023] The test strips of the present invention do not require the formation of a discrete exit port to permit air to escape from the device as sample enters the electrode chamber but instead uses a distributed exit along all of the edges of the mesh. As the sample fluid wicks along the mesh, air seeps out of the edges of the mesh all around the device underneath the top layer. The sample fluid does not seep out because the insulation layer imparts significant hydrophobicity to that part of the mesh. The liquid sample therefore remains in the central hydrophilic region.

[0024] The key to the performance achieved using the present invention is in the nature of the coating 17. This coating contains a filler which has both hydrophobic and hydrophilic surface regions, and in the case of a glucose test strip, an enzyme which can oxidize glucose, and a mediator which can transfer electrons from the enzyme

to the underlying conductive base layer 16. This coating is suitably formed by formulating an ink which contains the f iller, the enzyme and the mediator in a suitable carrier and using this ink to print the coating 17 onto the device.

[0025] A preferred filler for use in the coating 17 is silica. Silica is available in a variety of grades and with a variety of surface modifications. While all silica compounds tested resulted in a product which could measure glucose under some conditions, the superior performance characteristics of glucose test strip of the invention are obtained when a silica having a surface modification to render it partially hydrophobic is used. Materials of this type include Cab-O-Sil TS610, a silica which is modified by partial surface treatment with methyl dichlorosilane; Cab-o-Sil 530, a silica which is modified by full surface treatment with hexamethyl disilazane; Spherisorb C4 silica, which is surface modified with 4 carbon chains; and other similarly modified silicas, or combinations thereof. Silica with a surface modification which is too hydrophobic should be avoided, however, since it has been observed that C18-modified silica is too hydrophobic to form a printable ink.

[0026] During the process of manufacturing the ink of the invention, the particles are broken down by homogenization to expose hydrophilic inner portions of the silica particles. The actual particles present in the ink therefore have both hydrophilic and hydrophobic regions. The hydrophilic regions form hydrogen bonds with each other and with water.

[0027] When this material is formulated into an ink as described below in Example 1, and screen printed onto the conductive base layer 16, the dual nature of the material causes it two form layers of two-dimensional networks which take form as a kind of honeycomb. On rehydration, this layer does not break up, but swells to form a gelled reaction zone in the vicinity of the underlying conductive base layer 16. Reactants such as enzyme, mediator and glucose move freely within this zone, but interfering species such as red blood cells containing oxygenated hemoglobin are excluded. This results in a device in which the amount of current generated in response to a given amount of glucose varies by less than 10 percent over a hematocrit range of 40 to 60 %, and which is thus substantially insensitive to the hematocrit of the sample, and in fact performs substantially the same in blood as in a cell-free control solution. (Figs. 3A-C, Fig. 4 and Fig. 5A - 5C)

[0028] Furthermore, the gelled reaction zone presents a greater barrier to entry of blood analytes such as glucose which makes the device diffusion, rather than kinetically limited. This leads to a device in which the measured current varies by less than 10 percent over a temperature range from 20°C to 37°C and which is thus essentially temperature independent. (Figs. 6A and 6B)

[0029] When making a glucose test strip, the working layer is advantageously formed from an aqueous composition containing 2 to 10 % by weight, preferably 4 to 10 % and more preferably about 4.5 % of a binder such as hydroxyethylcellulose or mixtures of hydroxyethylcellulose with alginate or other thickeners; 3 to 10 % by weight, preferably 3 to 5 % and more preferably about 4 % silica; 8 to 20 % by weight, preferably 14 to 18 % and more preferably about 16 % of a mediator such as ferricyanide; and .4 to 2 % by weight, preferably 1 to 2 % and more preferably about 1.6 % of an enzyme such as glucose oxidase, assuming a specific activity of about 250 units/mg, or about 1000 to 5000 units per gram of ink formulation.

[0030] The working layer may also include additional ingredients without departing from the scope of the invention. For example, the nonconducting layer may include an antifoam. In addition, the nonconducting layer may be formulated with a buffering agent to control the pH of the reaction zone. The pH may be maintained at a level within the range from about pH 3 to pH 10. It is of particular utility to maintain the pH of the device at a level above 8 because at this pH oxygen bound to hemoglobin is not released. Further, at this pH, the reaction rate of glucose oxidase with oxygen is very low. Thus, selection of an appropriate pH can further stabilize the performance of the test strip against the effects of varying hematocrit.

[0031] While a preferred embodiment of the invention is a glucose test strip as described above, the test strips of the invention which include a first working coating disposed over the conductive base layer, said first working coating comprising a filler having both hydrophobic and hydrophilic surface regions. For example, a fructosamine test strip could include two layers disposed over the conductive base layer. The first, lower layer is formed from an ink comprising a carbonate buffer (pH>10) in a silica mix substantially as described in Example 7 but without enzyme, mediator or citrate buffer. The second, upper layer is formed form an ink further comprising an oxidant such a ferricyanide.

[0032] Fig. 7 shows an alternative embodiment of the invention. In this embodiment, a second working layer 71 is disposed over the first working layer 17. This layer is formed from a composition which is identical to the first working layer except that the enzyme or both the enzyme and the mediator are omitted. This layer further isolates the conductive base layer from contact with oxygen-carrying red blood cells, thus reducing the effects of oxygen. Furthermore, to the extent that enzyme may tend to diffuse away from the surface of the electrode during the course of the measurement, such a layer containing mediator can provide an increased region in which it will have mediator available for the transfer of electrons.

EXAMPLE 1

[0033] A non-conducting formulation for preparation of the working layer 17 was made as follows. 100 ml of

20 mM aqueous trisodium citrate was adjusted to pH 6 by the addition of 0.1 M citric acid. To this 6 g of hydroxyethyl cellulose (HEC) was added and mixed by homogenization. The mixture was allowed to stand overnight to allow air bubbles to disperse and then used as a stock solution for the formulation of the coating composition.

[0034] 2 grams Cab-o-Sil TS610 silica and 0.1 grams of Dow Corning antifoam compound was gradually added by hand to 50 grams of the HEC solution until about 4/5 of the total amount had been added. The remainder was added with mixing by homogenization. The mixture was then cooled for ten minutes in a refrigerator. 8 g of potassium hexacyanoferrate (III) was then added and mixed until completely dissolved. Finally, 0.8 g of glucose oxidase enzyme preparation (250 Units/mg) was added and then thoroughly mixed into the solution. The resulting formulation was ready for printing, or could be stored with refrigeration.

EXAMPLE 2

[0035] To prepare glucose test strips using the ink formulation of Example 1, a series of patterns are used to screen print layers onto a 330 micron polyester substrate (Melinex 329). The first step is the printing of carbon pads. An array of 10 X 50 pads of carbon is formed on the surface of the polyester substrate by printing with EC2 carbon. (Ercon) The printed substrate is then passed through a heated dryer, and optionally cured at elevated temperature (e.g. 70°C) for a period of 1 to 3 weeks.

[0036] Next, an array of silver/silver chloride connecting tracks and contacts is printed onto the substrate using ERCON R-414 (DPM-68)1.25 bioelectrode sensor coating material and dried. One working track which makes contact with the carbon pad and one reference track is printed for each carbon pad in the array.

[0037] A dielectric layer is then printed using ERCON R488-B(HV)-B2 Blue and dried. The dielectric layer is printed in a pattern which covers substantially all of each device, leaving only the contacts, the tip of the reference electrode and the carbon pads uncovered.

[0038] On top of the dielectric layer the ink of Example 1 is used to form a working layer overlaid on top of each conductive carbon pad.

[0039] Polyester mesh strips (Scrynel PET230 HC) are then laid down across the substrate in lines, covering the reactions areas exposed by the windows in the dielectric. An 5 mm wide polyester strip (50 microns thick) is then applied over the top of the mesh strips, and the edges of the electrodes are heat sealed. Finally, the substrate is cut up to provide 50 individual electrodes, for example having a size of 5.5 mm wide and 30 mm long.

EXAMPLE 3

[0040] Test strips manufactured using the ink formulation of Example 1 in the manner described in Example 2 were placed in a test meter with an applied voltage of 500 mV and used to test blood samples having varying glucose concentrations and hematocrits ranging from 40% to 60%. Figs. 3A-3C show the current measured 25 seconds after applying the voltage as a function of the glucose concentration, and Fig. 4 plots the slope of the glucose response as a function of hematocrit. As can be seen, the indicators produce highly reproducible current levels which are essentially independent of hematocrit.

EXAMPLE 4

[0041] Glucose test strips in accordance with the invention were made in accordance with Example 2, except the non-conductive layer was formed with 7 g Spherisorb C4 and 1 g Cab-o-Sil TS610. This formulation was laid down on three different types of carbon-containing conductive base layers as follows:

A: Ercon EC1
B: Ercon EC2
C: Ercon EC2 on top of Acheson Carbon, Electrodag 423 SS.

These test strips were used to measure varying levels of glucose in either a control solution (One Touch Control Solution, Lifescan Inc.) containing glucose in an inert solution or in blood at an applied voltage of 425 mV. The current observed 25 seconds after the voltage was applied was measured. Figs. 5A - 5C show the results obtained for the three formulations, A, B, and C, respectively. In all cases, the slope of the line showing the response of the meter to different glucose concentrations was essentially the same whether the measurements were made in blood or the control solution. Thus, this further demonstrates the independence of the test strips of the invention from the oxygen content and hematocrit of the sample, as well as the ability to use various materials as the conductive base layer.

EXAMPLE 5

[0042] Test strips prepared in accordance with Example 2 were tested at two different sample temperatures, namely 37 °C and 20 °C using an applied voltage of 425 mV. Figs. 6A and 6B show the current measured 25 seconds after applying the voltage as a function of glucose concentration. As can be seen, the slopes of the two lines are essentially identical (0.1068 at 20 °C versus 0.1009 at 37 °C), thus demonstrating that the test strips provide essentially temperature-independent behavior over a temperature range from ambient to physiological temperatures.

EXAMPLE 6

[0043] The current transient was measured for a test strip prepared in accordance with Example 2 and for a commercial test strip made with a carbon-containing ink. The results are shown in Figs. 8A and 8B. As shown, the,test strip of the invention (Fig. 8A) provides a very flat transient which maintains more than 50% of the peak current for a period of more than 25 seconds after the initial response from the test strip. In contrast, the carbon-based electrode exhibited an almost immediate decay in the current, having lost 50% of the peak current in a period of the first 1 to 2 seconds after the initial response from the test strip. This makes timing of the measurement difficult if peak current values are to be captured, or reduces the dynamic range of the meter if current must be measured after substantial decay has occurred. Thus, the test strips of the invention are advantageous in that the current generated in response to a given amount of glucose decays by less than 50% in the 5 seconds following peak current generation.

EXAMPLE 7

[0044] An ink for printing glucose test strips in accordance with the invention was formulated as follows:

67.8 g 20 mM Citrate buffer, pH 6
0.68 g Polyvinyl alcohol (MW 85,000-146,000, 88% hydrolysed)
0.68 g of Polyvinyl pyrrolidone-vinyl acetate
0.42 g of Dow Corning DC1500 antifoam
3.4 g of hydroxyethyl cellulose (Natrosol 250G, Hercules)
5.5 g of surface modified silica (Cabo-Sil TS 610, Cabot)
1.5 g glucose oxidase
20.0 g Potassium Ferricyanide.

Claims

1. A disposable test strip for use in a test meter of the type which receives a disposable test strip and a sample of blood and performs an electrochemical analysis of the amount of glucose in the sample, comprising:

   (a) a substrate (10);
   (b) a reference electrode (14');
   (c) a working electrode (22), said working electrode comprising a conductive base layer (16) disposed on the substrate (10) and a first working coating (17) disposed over the conductive base layer (16), said first working coating (17) comprising a filler having both hydrophobic and hydrophilic surface regions;
   (d) means (14, 15) for making an electrical connection between the reference and working electrode and a glucose test meter.

2. The test strip of claim 1, wherein the conductive base layer (16) comprises conductive carbon.

3. The test strip of claim 1 or 2, wherein the first working coating (17) is non-conductive.

4. The test strip according to any preceding claim, wherein the first working coating (17) forms a network over the conductive base layer (16) upon drying.

5. The test strip of claim 4, wherein the first working coating (17) on rehydration swells to form a gelled reaction zone on the conductive base layer (16) through which reactants can move freely but from which red blood cells are excluded.

6. The test strip of any preceding claim, wherein the filler is silica.

7. The test strip of claim 6, wherein the silica has been modified by surface treatment to render it partly hydrophobic.

8. The test strip of claim 7, wherein the silica is Cabo-Sil TS610 a silica which has been rendered partially hydrophobic by partial surface treatment with methyl dichlorosilane.

9. The test strip according to any preceding claim , which is for detection of glucose and wherein the first working coating (17) further comprises an enzyme effective to oxidise glucose and a mediator effective to transfer electrons from the enzyme to the conductive base layer (16).

10. The test strip of claim 9, wherein the enzyme is glucose oxidase.

11. The test strip of claim 9 or 10, wherein the mediator is ferricyanide.

12. The test strip of any of claims 9 to 11, wherein the first working layer is formed from an aqueous composition comprising 2 to 10% by weight of a binder; 3 to 10% by weight of silica; 8 to 20% by weight of a mediator; and 1000 to 5000 units per gram of the aqueous composition.

13. The test strip of any preceding claim, further comprising an insulating mask (18) disposed on the substrate (10) that leaves a portion of the conductive base layer (16), the reference electrode (14') and contacts (11, 12 and 13) exposed, the first working coating (17) overlying the insulating mask (18) and

making contact with the conductive base layer (16).

14. The test strip according to any of claims 9-13, further comprising a second working layer (71) comprising silica, a binder and a mediator, but no glucose-oxidizing enzyme.

15. The test strip of any preceding claim, further comprising a polyester mesh (21) over the working electrode (22).

16. The test strip of claim 15, further comprising a top cover (23) over the polyester mesh (21) for preventing the splashing of a blood sample.

17. A method for making the disposable test strip of any preceding claim, comprising the steps of:

applying to a substrate (10) a working electrode track (15) and a reference electrode track (14) terminating in a reference electrode (14');
applying a conductive base layer (16) in contact with the working electrode track (15); and
applying a first working coating (17) over the conductive base layer (16), wherein the working coating (17) comprises a filler having both hydrophobic and hydrophilic surface regions.

18. The method of claim 17, wherein:

an insulating mask (18) is applied to the substrate (10) leaving a portion of the conductive base layer (16), the reference electrode (14') and contacts (11, 12 and 13) exposed; and
the first working coating (17) is applied so as to overlie the insulating mask (18) and make contact with the conductive base layer (16).

Patentansprüche

1. Ein wegwerfbarer Teststreifen zur Verwendung in einem Testmeßgerät (test meter) des Typs, der einen wegwerfbaren Teststreifen und eine Blutprobe aufnimmt und eine elektrochemische Analyse der Menge an Glukose in der Probe durchführt, umfassend:

(a) ein Substrat (10);
(b) eine Referenzelektrode (14');
(c) eine Arbeitselektrode (22), wobei die Arbeitselektrode eine leitende Grundschicht (16), angeordnet auf dem Substrat (10), und eine erste Arbeitsbeschichtung (17), angeordnet über der leitenden Grundschicht (16), umfaßt, wobei die erste Arbeitsbeschichtung (17) ein Füllmaterial mit sowohl hydrophoben als auch hydrophilen Oberflächenregionen umfaßt;
(d) Mittel (14, 15) zum Herstellen einer elektrischen Verbindung zwischen der Referenz- und der Arbeitselektrode und einem Glukose-Testmeßgerät.

2. Teststreifen nach Anspruch 1, wobei die leitende Grundschicht (16) leitenden Kohlenstoff umfaßt.

3. Teststreifen nach Anspruch 1 oder 2, wobei die erste Arbeitsbeschichtung (17) nichtleitend ist.

4. Teststreifen nach einem vorangehenden Anspruch, wobei die erste Arbeitsbeschichtung (17) ein Netzwerk über der leitenden Grundschicht (16) nach einer Trocknung bildet.

5. Teststreifen nach Anspruch 4, wobei die erste Arbeitsbeschichtung (17) beim Rehydratisieren quillt, um eine gelierte Reaktionszone auf der leitenden Grundschicht (16) zu bilden, durch welche sich Reaktanten frei bewegen können, von der aber rote Blutkörperchen ausgeschlossen sind.

6. Teststreifen nach einem vorangehenden Anspruch, wobei das Füllmaterial Siliciumdioxid ist.

7. Teststreifen nach Anspruch 6, wobei das Siliciumdioxid durch Oberflächenbehandlung modifiziert worden ist, um es teilweise hydrophob zu machen.

8. Teststreifen nach Anspruch 7, wobei das Siliciumdioxid Cab-o-Sil TS 610 ist, ein Siliciumdioxid, das durch partielle Oberflächenbehandlung mit Dichlordimethylsilan teilweise hydrophob gemacht worden ist.

9. Teststreifen nach einem vorangehenden Anspruch, der zum Nachweis von Glukose dient, und bei dem die erste Arbeitsbeschichtung (17) weiterhin ein Enzym, das dahingehend wirkt, Glukose zu oxidieren, und einen Mediator umfaßt, der dahingehend wirkt, Elektronen von dem Enzym auf die leitende Grundschicht (16) zu übertragen.

10. Teststreifen nach Anspruch 9, wobei das Enzym Glukoseoxidase ist.

11. Teststreifen nach Anspruch 9 oder 10, wobei der Mediator Ferricyanid ist.

12. Teststreifen nach einem der Ansprüche 9 bis 11, wobei die erste Arbeitsschicht aus einer wäßrigen Zusammensetzung gebildet wird, umfassend 2 bis 10 Gew.% eines Bindemittels; 3 bis 10 Gew.% Siliciumdioxid; 8 bis 20 Gew.% eines Mediators; und 1000 bis 5000 Einheiten pro Gramm der wäßrigen Zusammensetzung.

13. Teststreifen nach einem vorangehenden Anspruch, weiterhin umfassend eine Isoliermaske (18), angeordnet auf dem Substrat (10), die einen Teil der leitenden Grundschicht (16), die Referenzelektrode (14') und Kontakte (11, 12 und 13) exponiert läßt, wobei die erste Arbeitsbeschichtung (17) über der Isoliermaske (18) liegt und mit der leitenden Grundschicht (16) Kontakt herstellt.

14. Teststreifen nach einem der Ansprüche 9-13, weiterhin umfassend eine zweite Arbeitsschicht (71), umfassend Siliciumdioxid, ein Bindemittel und einen Mediator, aber kein Glukose-oxidierendes Enzym.

15. Teststreifen nach einem vorangehenden Anspruch, weiterhin umfassend ein Polyesternetz (21) über der Arbeitselektrode (22).

16. Teststreifen nach Anspruch 15, weiterhin umfassend eine obere Abdeckung (23) über dem Polyesternetz (21) zum Verhindern des Herausspritzens einer Blutprobe.

17. Ein Verfahren zum Herstellen des wegwerfbaren Teststreifens nach einem vorangehenden Anspruch, umfassend die Schritte:

Aufbringen auf ein Substrat (10) eine Arbeitselektrodenspur (15) und eine Referenzelektrodenspur (14), die in einer Referenzelektrode (14') endet;
Aufbringen einer leitenden Grundschicht (16) in Kontakt mit der Arbeitselektrodenspur (15); und
Aufbringen einer ersten Arbeitsbeschichtung (17) über der leitenden Grundschicht (16), wobei die Arbeitsbeschichtung (17) ein Füllmaterial mit sowohl hydrophoben als auch hydrophilen Oberflächenregionen umfaßt.

18. Verfahren nach Anspruch 17, wobei:

eine Isoliermaske (18) auf das Substrat (10) aufgebracht wird, wobei ein Teil der leitenden Grundschicht (16), die Referenzelektrode (14') und Kontakte (11, 12 und 13) exponiert gelassen werden; und
die erste Arbeitsbeschichtung (17) aufgetragen wird, so daß sie über der Isoliermaske (18) liegt und mit der leitenden Grundschicht (16) Kontakt herstellt.

Revendications

1. Bande de test jetable pour l'utilisation dans un contrôleur du type qui reçoit une bande de test jetable et un échantillon de sang et qui effectue une analyse électrochimique de la quantité de glucose dans l'échantillon, comprenant :

(a) un substrat (10) ;
(b) une électrode de référence (14') ;
(c) une électrode à étudier (22), ladite électrode à étudier comprenant une couche de base conductrice (16) placée sur le substrat (10) et un premier revêtement à étudier (17) placé sur la couche de base conductrice (16), ledit premier revêtement à étudier (17) comprenant une charge ayant des régions de surface hydrophobes et hydrophiles ;
(d) des moyens (14, 15) pour réaliser une connexion électrique entre les électrodes de référence et à étudier et un contrôleur de glucose.

2. Bande de test selon la revendication 1, dans laquelle la couche de base conductrice (16) comprend du carbone conducteur.

3. Bande de test selon la revendication 1 ou 2, dans laquelle le premier revêtement à étudier (17) est non conducteur.

4. Bande de test selon l'une quelconque des revendications précédentes, dans laquelle le premier revêtement à étudier (17) forme un réseau sur la couche de base conductrice (16) en séchant.

5. Bande de test selon la revendication 4, dans laquelle le premier revêtement à étudier (17) gonfle pendant la réhydratation, pour former une zone de réaction gélifiée sur la couche de base conductrice (16), à travers laquelle les réactifs peuvent se déplacer librement, mais de laquelle les globules rouges sont exclus.

6. Bande de test selon l'une quelconque des revendications précédentes, dans laquelle la charge est de la silice.

7. Bande de test selon la revendication 6, dans laquelle la silice a été modifiée par un traitement de surface pour la rendre partiellement hydrophobe.

8. Bande de test selon la revendication 7, dans laquelle la silice est une silice cab-o-SiLTS610 qui a été rendue partiellement hydrophobe par un traitement de surface partiel avec du dichlorosilane de méthyle.

9. Bande de test selon l'une quelconque des revendications précédentes, qui est destinée à la détection du glucose et dans laquelle le premier revêtement à étudier (17) comprend en outre une enzyme efficace pour oxyder le glucose et un médiateur effica-

ce pour transférer les électrons de l'enzyme vers la couche de base conductrice (16).

10. Bande de test selon la revendication 9, dans laquelle l'enzyme est de l'oxydase de glucose.

11. Bande de test selon la revendication 9 ou 10, dans laquelle le médiateur est du ferricyanure.

12. Bande de test selon l'une quelconque des revendications 9 à 11, dans laquelle le premier revêtement à étudier est formé à partir d'une composition aqueuse comprenant de 2 à 10 % en poids d'un liant ; de 3 à 10 % en poids de silice ; de 8 à 20 % en poids d'un médiateur ; et de 1000 à 5000 unités par gramme de la composition aqueuse.

13. Bande de test selon l'une quelconque des revendications précédentes, comprenant en outre un masque isolant (18) placé sur le substrat (10) qui laisse une portion de la couche de base conductrice (16), de l'électrode de référence (14') et des contacts (11, 12 et 13) exposée, le premier revêtement à étudier (17) recouvrant le masque isolant (18) et créant un contact avec la couche de base conductrice (16).

14. Bande de test selon l'une quelconque des revendications 9 à 13, comprenant en outre une seconde couche à étudier (71) comprenant de la silice, un liant et un médiateur, mais pas d'enzyme oxydant le glucose.

15. Bande de test selon l'une quelconque des revendications précédentes, comprenant en outre une maille de polyester (21) sur l'électrode à étudier (22).

16. Bande de test selon la revendication 15, comprenant en outre une enveloppe supérieure (23) sur la maille de polyester (21) pour empêcher l'éclaboussure d'un échantillon de sang.

17. Procédé de fabrication de la bande de test jetable selon l'une quelconque des revendications précédentes, comprenant les étapes consistant à :

appliquer sur un substrat (10) un cheminement d'électrode à étudier (15) et un cheminement d'électrode de référence (14) se terminant dans une électrode de référence (14') ;
appliquer une couche de base conductrice (16) en contact avec le cheminement de l'électrode à étudier (15) ; et
appliquer un premier revêtement à étudier (17) sur la couche de base conductrice (16), dans lequel le revêtement à étudier (17) comprend une charge ayant des régions de surface hydrophobes et hydrophiles.

18. Procédé selon la revendication 17, dans lequel :

un masque isolant (18) est appliqué sur le substrat (10), laissant une portion de la couche de base conductrice (16), de l'électrode de référence (14') et des contacts (11, 12 et 13) exposée ; et
le premier revêtement à étudier (17) est appliqué de manière à recouvrir le masque isolant (18) et à créer un contact avec la couche de base conductrice (16).

Fig. 1A

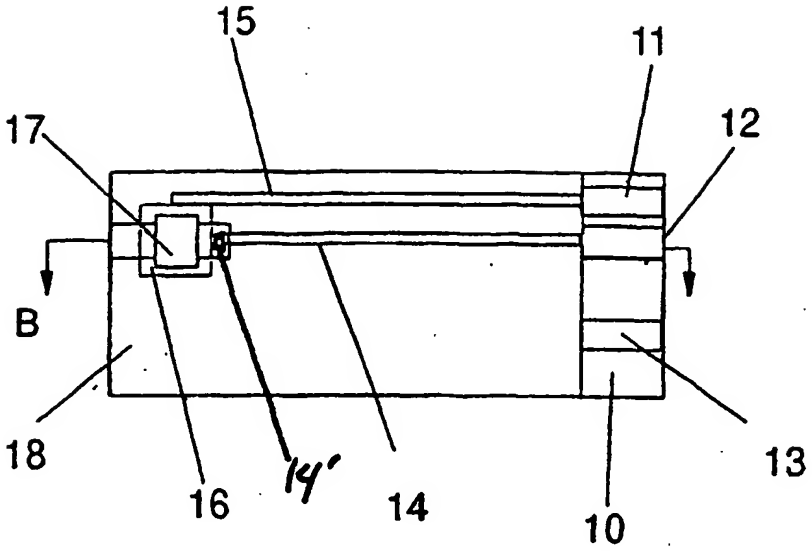
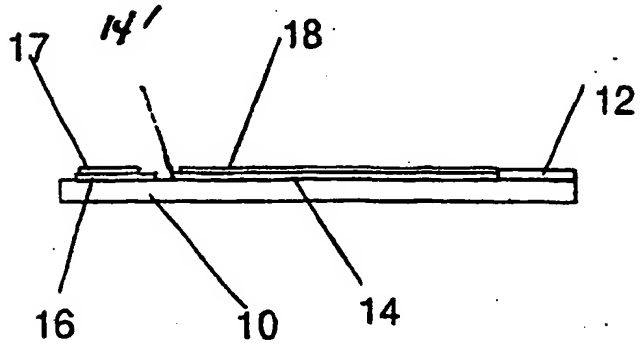


Fig. 1 B



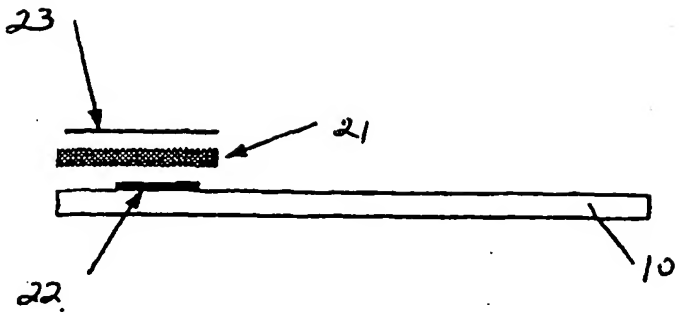

23
21
22
10

Fig 2

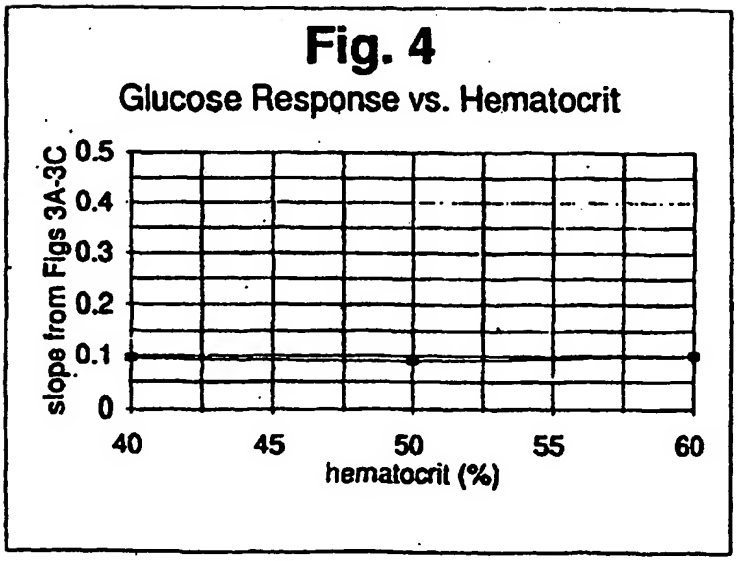


Fig. 4
Glucose Response vs. Hematocrit
slope from Figs 3A-3C
0.5
0.4
0.3
0.2
0.1
0
40
45
50
55
60
hematocrit (%)

Fig. 3A 60 % Haematocrit, measured at 500 mV

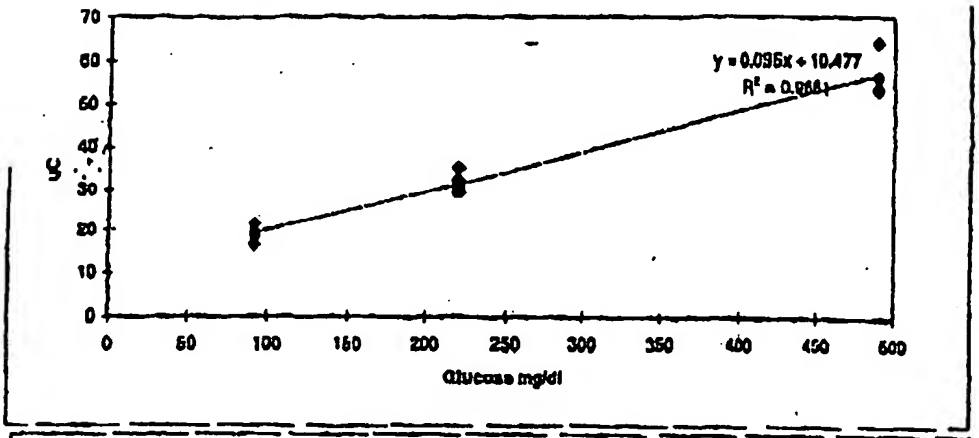


Fig. 3B 50% Haematocrit, measured at 500mV

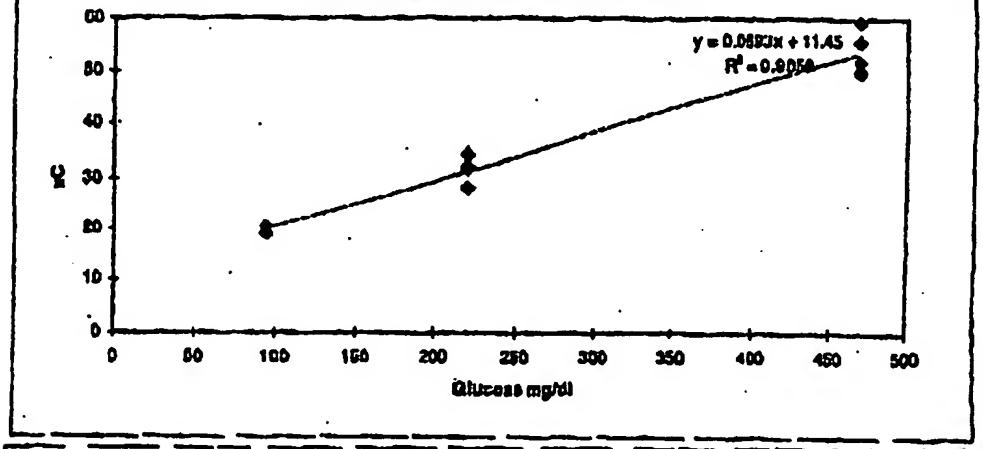


Fig. 3C 40% Haematocrit, measured at 500 mV

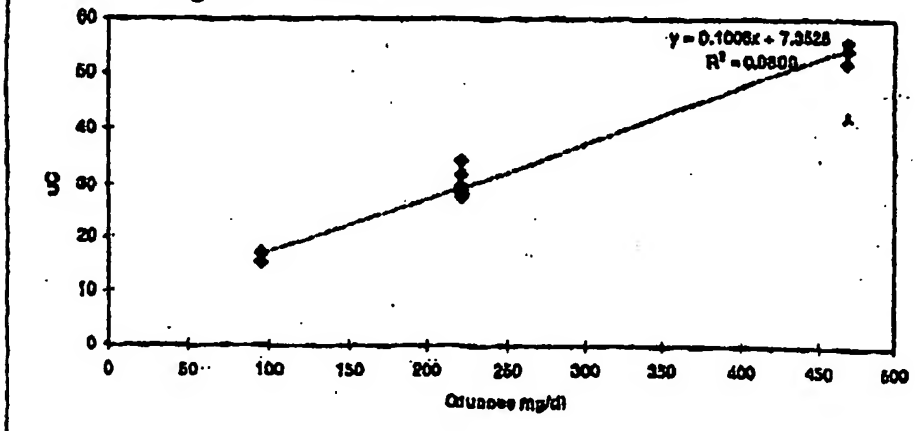


Fig. 5A

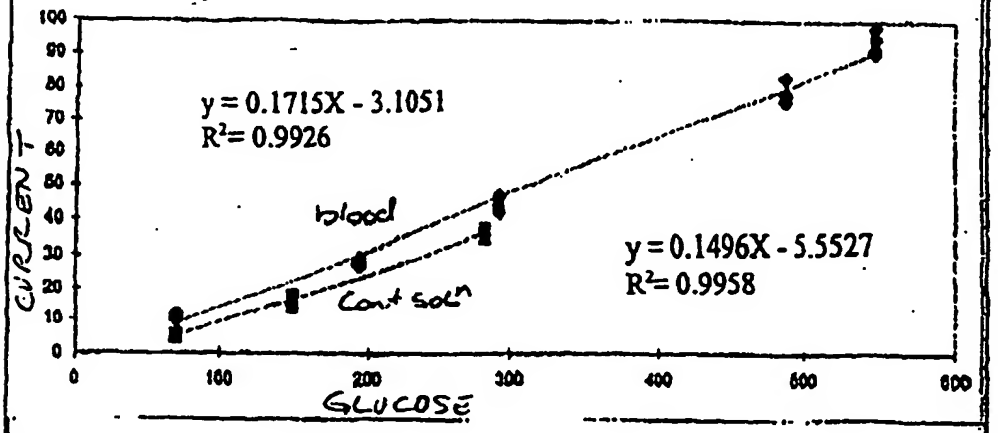


Fig. 5B

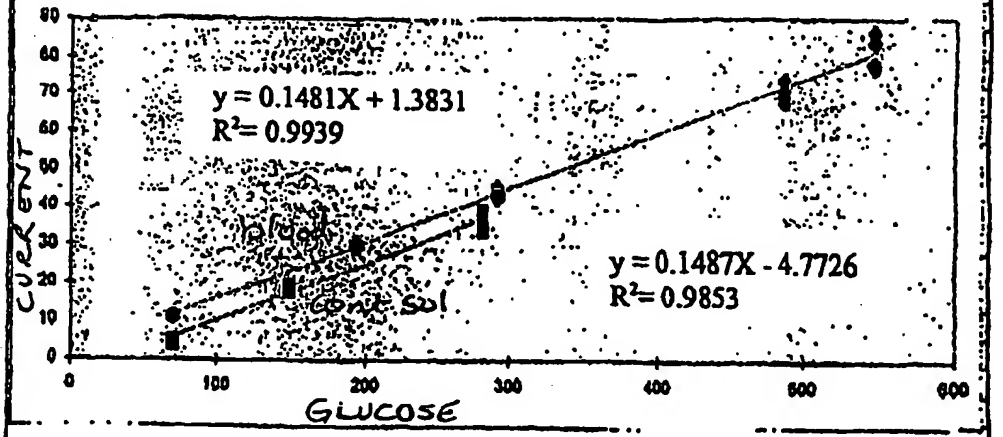


Fig. 5C

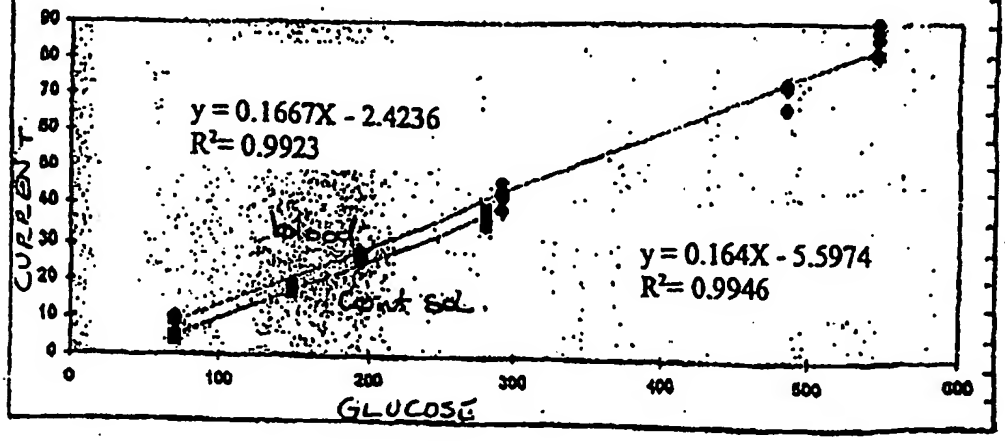


Fig. 6A

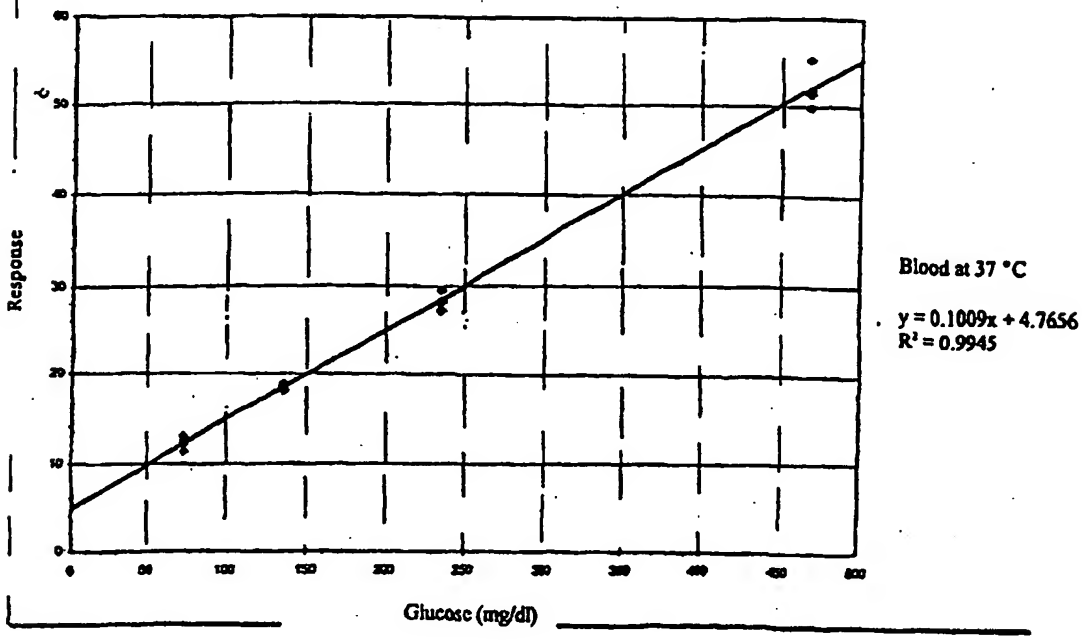

Response
Glucose (mg/dl)
Blood at 37 °C
y = 0.1009x + 4.7656
R² = 0.9945

Fig. 6B

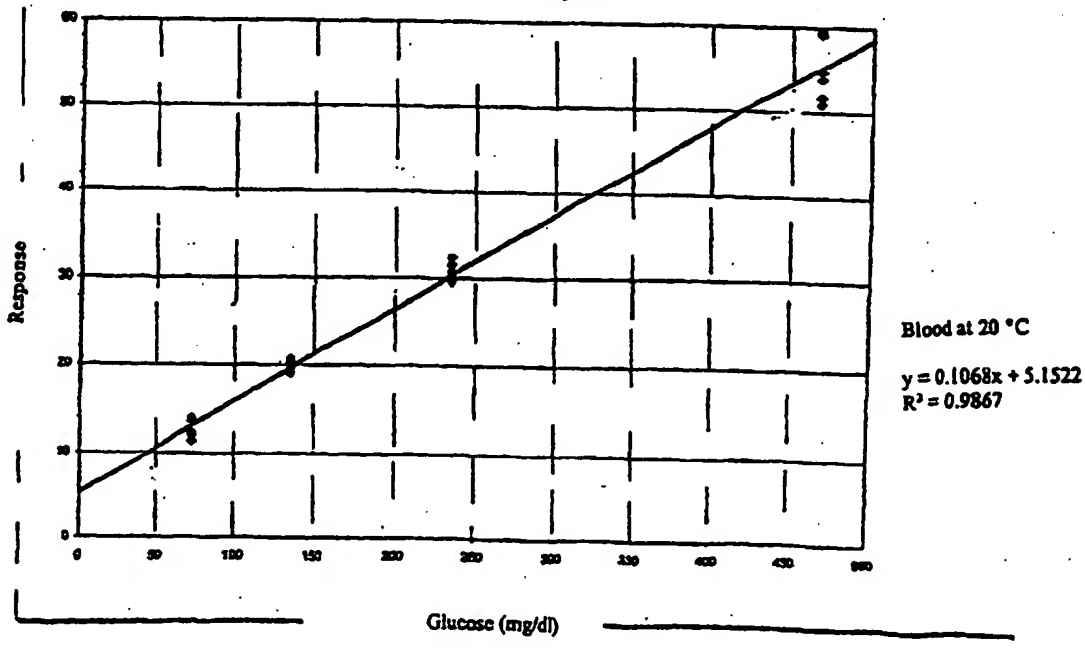

Response
Glucose (mg/dl)
Blood at 20 °C
y = 0.1068x + 5.1522
R² = 0.9867

Fig. 7

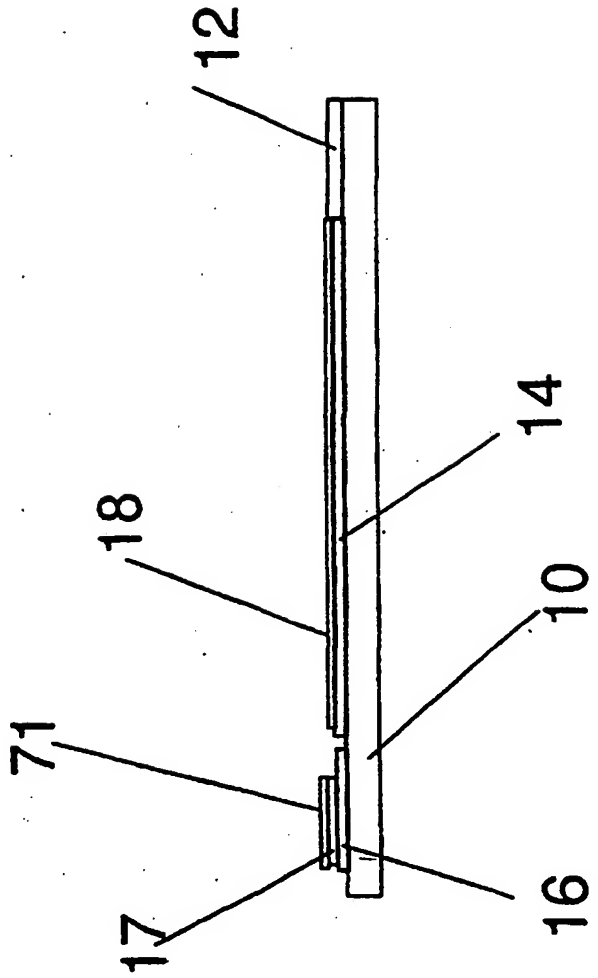


Fig 8A

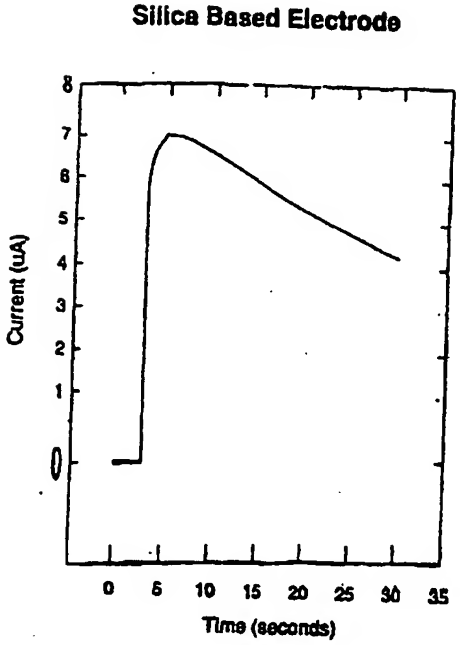
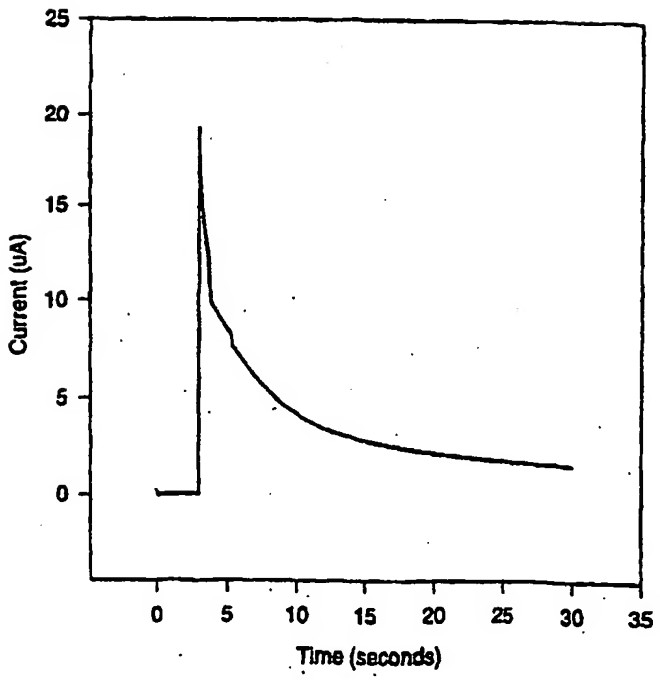

Silica Based Electrode
Current (uA)
8
7
6
5
4
3
2
1
0
0
5
10
15
20
25
30
35
Time (seconds)

Fig 8B


Carbon Based Electrode
Current (uA)
25
20
15
10
5
0
0
5
10
15
20
25
30
35
Time (seconds)